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**REMARKS**

The present application was originally filed with 31 Claims. In a Restriction Requirement mailed October 2, 2003, the Examiner restricted the Claims into five Groups, with Group I containing Claims 1-6, 11, 14-29, and 31, directed to methods and systems for creating libraries of nucleic acid sequences; Group II containing Claim 7, directed to a library; Group III containing Claims 8, 9, and 30, directed to methods for screening libraries for a protein with an increase in a property of interest; Group IV containing Claim 10, directed to a protein; and Group V containing Claims 12 and 13, directed to methods for improving a desired parameter of a protein of interest. In a Response filed October 20, 2003, Applicants elected the Claims in Group I (Claims 1-6, 11, 14-29, and 31), with traverse, cancelled Claims 8-10, 12, 13 and 30 without prejudice. Thus, Claims 1-7, 11, 14-29 and 31 were pending in the present application.

In the present Office Action, the Examiner indicates that Group II (Claim 7) has not been joined with Group I (Claims 1-6, 11, 14-29 and 31). Claim 7 has been cancelled without prejudice. Applicants reserve the right to pursue the original and/or broader and/or narrower Claims in additional application(s). The Examiner's rejections are addressed in the following order:

- 1) Claim 11 stands rejected under 35 U.S.C. §101, as allegedly being directed to non-statutory patentable subject matter;
- 2) Claims 1-6, 11, 14-29, and 31 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite; and
- 3) Claims 1-6, 11, 14-29, and 31 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Marr et al. (US Pat. No. 5,701,256).

**1) The Claims Recite Patentable Subject Matter**

The Examiner has rejected Claim 11, under 35 U.S.C. §101, as allegedly being directed to non-statutory subject matter. In particular, the Examiner argues that in view of the Specification and the absence of physical elements, the nucleic acid sequence, probability matrix, and constraint vector merely reflect data. Applicants believe that the Claim covers patentable subject matter as filed. Nonetheless, in order to further their business interests and the prosecution of the present application, yet without acquiescing to the Examiner's arguments, Applicants have amended Claim 11 to recite that the probability matrix is generated by a computer. Applicants have cancelled Claim 24 and amended the preamble to recite a "method," rather than a system. Applicants respectfully submit that these amendments find more than sufficient support in the Specification as

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filed and do not introduce new matter. As amended Claim 11 clearly encompasses patentable subject matter, Applicants respectfully request that this rejection be withdrawn.

### 2) The Claims are Definite

The Examiner has rejected Claims 1-6, 11, 14-19, and 31 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. In particular, the Examiner argues that Claim 11 is indefinite for failing to include any physical devices in the Claim. In regards to Claims 23 and 25, the Examiner argues that the limitation of "the probability matrix is an algorithm"/"the constraint vector is an algorithm" is confusing. Applicants believe that the Claims as filed are definite. Nonetheless, as indicated previously, Claim 11 has been amended to recite the use of a computer to determine the probability matrix. Claims 23 and 25 have been amended to recite that the probability matrix and constraint vectors, respectively, are generated using a computer. Again, as there is more than sufficient support in the Specification as filed for these amendments, Applicants respectfully submit that no new matter has been added. As the Claims are definite, Applicants respectfully request that this rejection be withdrawn.

### 3) The Claims are Novel

The Examiner has rejected Claims 1-6, 11, 14-29, and 31 under 35 U.S.C. §102(b), as allegedly being anticipated by Marr et al. (US Pat. No. 5,701,256). The Examiner argues that the search information generated using the methods of the Marr et al. Patent is "...then transferred to a DNA library for construction (Columns 12-14, beginning on line 63)." (Office Action, page 6). Applicants must respectfully disagree, as the Marr et al. Patent simply indicates that the search methods provided by the Marr et al. Patent may be used to search libraries. In contrast, the presently claimed invention clearly is directed toward methods for the *generation* of libraries. There is no teaching in the Marr et al. Patent about how to generate libraries, particularly libraries in which substitutions of interest are incorporated into the libraries. Rather, the Marr et al. Patent describes search methods to identify substitutions in sequences. As the Marr et al. Patent fails to disclose each and every element of the claimed invention as required for anticipation<sup>2</sup>, Applicants respectfully request that this rejection be withdrawn and the pending Claims passed to allowance.

<sup>2</sup> Anticipation is established only when a single prior art reference discloses, expressly or under principles of inherency, each and every element of a claimed invention." (*RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 221 USPQ 385, 388 (Fed. Cir. 1984)).


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**CONCLUSION**

All grounds of rejection and objection of the Office Action of December 15, 2003, having been addressed, reconsideration of the application is respectfully requested. Applicants respectfully submit that the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-5838.

Respectfully submitted,

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